

CLAIMS

What is claimed is:

1. A method of detecting an activity of a COX-2 enzyme in a subject, comprising:
 - a) obtaining a sample of the subject; and
 - b) detecting a COX-2 specific metabolite of a 2-arachidonylglycerol in the sample, wherein the presence of the COX-2 specific metabolite in the sample indicates the activity of the COX-2 enzyme in the subject.
2. The method of claim 1, wherein the metabolite comprises a prostaglandin-glycerol ester.
3. The method of claim 1, wherein the metabolite is selected from a group consisting of: prostaglandin H₂-glycerol ester, prostaglandin E₂-glycerol ester, 15-keto-prostaglandin E₂-glycerol ester, 13,14-dihydro-15-keto-prostaglandin E₂-glycerol ester, prostaglandin D₂-glycerol ester, prostaglandin F_{2α}-glycerol ester, thromboxane A₂-glycerol ester, thromboxane B₂-glycerol ester, prostacyclin-glycerol ester, 6-keto-prostaglandin F_{1α}-glycerol ester, prostaglandin A₂-glycerol ester, and prostaglandin B₂-glycerol ester.
4. The method of claim 1, wherein the metabolite comprises a 6-keto-prostaglandin F_{1α}-glycerol ester.
5. The method of claim 1, wherein the subject comprises a human.
6. The method of claim 1, wherein the subject comprises a non-human mammal.
7. The method of claim 1, wherein the subject comprises a cultured cell.
8. The method of Claim 1, wherein the detecting step includes generating a mass spectrum of the metabolite.
9. The method of Claim 1, wherein the detecting step includes contacting the metabolite with an antibody.
10. The method of claim 1, wherein the sample comprises urine.

11. The method of claim 1, wherein the sample comprises plasma.
12. The method of Claim 1, wherein the sample is selected from a group consisting of: cerebrospinal fluid, saliva, sputum, bile, joint fluid, biopsy, and conditioned media from a cell culture.
- 5 13. A method of measuring an activity of a COX-2 enzyme in a subject, comprising:
 - a) obtaining a sample of the subject;
 - b) measuring an amount of a COX-2 specific metabolite of a 2-arachidonylglycerol in the sample; and
 - c) relating the amount of the COX-2 specific metabolite to the activity of the COX-2 enzyme.
- 10 14. The method of Claim 13, further comprising comparing the amount measured to a standard value.
15. The method of Claim 13, further comprising generating a standard curve.
- 15 16. The method of claim 13, wherein the metabolite comprises a prostaglandin-glycerol ester.
17. The method of claim 13, wherein the metabolite comprises a 6-keto-prostaglandin F_{1α}-glycerol ester.
18. The method of claim 13, wherein the subject comprises a human.
19. The method of Claim 13, wherein the measuring step includes generating a mass spectrum of the metabolite.
- 20 20. The method of claim 13, wherein the sample comprises urine.
21. The method of claim 13, wherein the sample comprises plasma.
22. The method of claim 13, wherein the sample is selected from a group consisting of: cerebrospinal fluid, saliva, sputum, bile, joint fluid, biopsy, and conditioned media from a cell culture.
- 25 23. A method of detecting an activity of a COX-2 enzyme in a subject, comprising:
 - a) obtaining a sample of the subject; and

b) detecting a metabolite of a COX-2 selective substrate in the sample, wherein the presence of the metabolite in the sample indicates the activity of the COX-2 enzyme in the subject.

24. The method of claim 23, further comprising measuring an amount of the metabolite in the sample.

25. The method of claim 24, further comprising relating the amount of the metabolite in the sample to the activity of the COX-2 enzyme in the subject.

26. The method of claim 23, wherein the metabolite comprises a prostaglandin-glycerol ester.

27. The method of claim 23, wherein the metabolite comprises a 6-keto-prostaglandin F_{1α}-glycerol ester.

28. The method of claim 23, wherein the subject comprises a human.

29. The method of claim 23, wherein the measuring step includes generating a mass spectrum of the metabolite.

30. The method of claim 23, wherein the sample comprises urine.

31. The method of claim 23, wherein the sample comprises plasma.

32. The method of claim 23, wherein the sample is selected from a group consisting of: cerebrospinal fluid, saliva, sputum, bile, joint fluid, biopsy, and conditioned media from a cell culture.

33. A method of detecting a COX-2 activity in a sample, comprising:

a) adding a COX-2 selective substrate to the sample; and

b) detecting a metabolite of the COX-2 selective substrate in the sample, wherein the presence of the metabolite indicates activity of the COX-2 enzyme in the sample.

34. The method of claim 33, wherein the COX-2 selective substrate comprises an arachidonylglycerol ester.

35. The method of claim 33, further comprising measuring an amount of the metabolite.
36. The method of claim 33, further comprising relating the amount of the metabolite to the activity of the COX-2 enzyme.
- 5 37. The method of claim 33, wherein the metabolite comprises a prostaglandin-glycerol ester.
38. The method of claim 33, wherein the metabolite is selected from a group consisting of: prostaglandin H₂-glycerol ester, prostaglandin E₂-glycerol ester, 15-keto-prostaglandin E₂-glycerol ester, 13,14-dihydro-15-keto-prostaglandin E₂-glycerol ester, prostaglandin D₂-glycerol ester, prostaglandin F_{2α}-glycerol ester, thromboxane A₂-glycerol ester, thromboxane B₂-glycerol ester, prostacyclin-glycerol ester, 6-keto-prostaglandin F_{1α}-glycerol ester, prostaglandin A₂-glycerol ester, and prostaglandin B₂-glycerol ester.
39. The method of claim 1, wherein the metabolite comprises a 6-keto-prostaglandin F_{1α}-glycerol ester.
- 15 40. A method of detecting a COX-2 activity in a subject, comprising:
- a) administering an effective amount of a COX-2 selective substrate to the subject;
 - b) detecting a metabolite of the COX-2 selective substrate in the subject,
- 20 wherein the presence of the metabolite indicates the COX-2 activity.
41. The method of claim 40, further comprising measuring a level of the metabolite.
42. The method of claim 41, further comprising relating the level of the metabolite to the COX-2 activity in the subject.
- 25 43. The method of claim 40, wherein the subject is a human.
44. The method of claim 40, wherein the metabolite comprises a prostaglandin glycerol ester.

45. The method of claim 40, further comprising obtaining a sample of the subject.
46. The method of claim 45, wherein the sample is urine, blood, plasma, cerebrospinal fluid, saliva, sputum, bile, joint fluid, or biopsy tissue.
47. The method of claim 40, further comprising relating the COX-2 activity to a clinical condition of the subject.
48. The method of claim 47, wherein the clinical condition comprises a tumor.
49. The method of claim 48, wherein the clinical condition comprises an inflammation.
50. A method of screening for a tumor in a subject in need thereof, comprising:
- a) obtaining a sample of the subject; and
 - b) detecting a COX-2 specific metabolite in the sample; wherein the presence of the COX-2 specific metabolite is indicative of the tumor in the subject.
51. The method of claim 50, wherein the subject is a human.
52. The method of claim 50, wherein the COX-2 specific metabolite comprises a prostaglandin glycerol ester.
53. The method of claim 50, further comprising measuring an amount of the COX-2 specific metabolite.
54. The method of claim 53, further comprising relating the amount of the COX-2 specific metabolite to a stage of the tumor.
55. A method of monitoring an anticancer treatment in a patient in need thereof, comprising:
- a) obtaining a first sample of a patient;
 - b) measuring a first amount of a COX-2 specific metabolite in the first sample;
 - c) obtaining a second sample of the patient after the anticancer treatment;
 - d) measuring a second amount of the COX-2 specific metabolite in the second sample; and

- e) determining a change in the second amount relative to the first amount, wherein the change indicates the effectiveness of the treatment.

56. The method of claim 55, wherein the COX-2 specific metabolite comprises a prostaglandin glycerol ester.

- 5 57. A method of detecting an inflammation in a subject in need thereof, comprising:
- a) obtaining a sample of the subject; and
 - b) detecting a COX-2 specific metabolite in the sample, wherein the presence of the COX-2 specific metabolite indicates the inflammation.

10 58. The method of claim 57, wherein the COX-2 specific metabolite comprises a prostaglandin glycerol ester.

59. The method of claim 57, further comprising measuring an amount of the COX-2 specific metabolite.

60. A method of monitoring an anti-inflammation treatment in a subject in need thereof, comprising:

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- a) obtaining a first sample of the subject;
 - b) measuring a first amount of a COX-2 specific metabolite in the first sample;
 - c) obtaining a second sample of the subject after the anti-inflammation treatment ;
 - d) measuring a second amount of the COX-2 specific metabolite in the second sample; and
 - e) determining a change in the second amount relative to the first amount, wherein the change indicates the effectiveness of the treatment.
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61. A composition comprising: a COX-2 selective metabolite including a label for detecting the metabolite.
62. The composition of Claim 61, wherein the label comprises an isotopic label.
63. The composition of Claim 61, wherein the COX-2 selective metabolite is selected from the group consisting of PGE₂-G, PGD₂-G, PGF₂-G, PGF_{2α}-G, PGH₂-G, PGJ₂-G, PGJ₂-G derivatives, 13,14-dihydro-15-keto-PGE₂-G, 15-keto-PGE₂-G, bicyclo-PGE₂-G, 11-HETE-G, 15-HETE-G, TxA₂-G and TxB₂-G
64. The composition of Claim 61, wherein the label comprises a non-positron emitting isotopic label.
65. The composition of Claim 61, wherein the label is ²H, ³H, ¹³C, or ¹⁴C.
66. The composition of Claim 61, wherein the label comprises a fluorescent label.
67. A process for making a COX-2 selective metabolite having a label comprising: reacting a COX metabolite with a labeled glycerol.
68. The process of Claim 67, wherein the label comprises an isotopic label.
69. The process of Claim 67, wherein the label comprises a nonpositron emitting label.
70. The process of Claim 67, wherein the label is ²H, ³H, ¹³C, or ¹⁴C.
71. The process of Claim 67, wherein the label comprises a fluorescent label.
72. A process for making an isolated COX-2 selective metabolite including a label comprising: reacting a labeled COX metabolite with glycerol.
73. The process of Claim 72, wherein the label comprises an isotopic label.
74. A process for making a labeled COX-2 selective metabolite, comprising: reacting a labeled 2-arachidonylglycerol with a COX-2 enzyme to form the labeled COX-2 selective metabolite.
75. The process of claim 74, wherein the label comprises an isotopic label.
76. The process of claim 74, further comprising isolating the labeled COX-2 selective metabolite.

77. The process of claim 74, further comprising reacting the labeled COX-2 selective metabolite with a secondary enzyme.

78. An article of manufacture comprising, packaged together:

- a) a vessel containing an isolated antibody against a COX-2 selective metabolite; and
- b) a set of instructions delineating a process of detecting an activity of a COX-2 enzyme.

79. An article of manufacture comprising, packaged together:

- a) a vessel containing at least one labeled COX-2 selective metabolite; and
- b) a set of instructions delineating a process of detecting an activity of a COX-2 enzyme.

80. An antibody that binds specifically to a prostaglandin glyceryl ester.

81. An antibody that binds specifically to a 6-keto-prostaglandin F_{1α}-glycerol ester.

82. A process of preparing an antigen for the manufacture of an antibody that binds specifically to a glyceryl-prostaglandin having one or more substituted cyclopentyl and ester moieties, comprising:

- a) protecting the substituted cyclopentyl and ester moieties of the glyceryl-prostaglandin;
- b) haptenizing the protected glyceryl-prostaglandin;
- c) deprotecting the one or more substituted cyclopentyl and ester moieties of the haptenized glyceryl-prostaglandin;
- d) purifying the haptenized glyceryl-prostaglandin.

83. The process of claim 82, further comprising manufacturing the antibody that binds specifically to the glyceryl-prostaglandin.

84. The process of claim 83, wherein the glyceryl-prostaglandin comprises a 6-keto-prostaglandin F_{1α}-glycerol ester.

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85. A composition comprising: a prostaglandin D₂-glycerol ester and pharmaceutically acceptable salts thereof.
86. A composition comprising: a 6-keto-prostaglandin F_{1α}-glycerol ester and pharmaceutically acceptable salts thereof.

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